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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/915,694	07/25/2001	Olga Bandman	PF-0379-1 DIV	1205

27904 7590 12/17/2002

INCYTE GENOMICS, INC.
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EXAMINER	
FRONDA, CHRISTIAN L	

ART UNIT	PAPER NUMBER
1652	8

DATE MAILED: 12/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/915,694	Bandman et al.
Examiner	**Art Unit**
Christian L. Fronda	1652

-- ***The MAILING DATE of this communication appears on the cover sheet with the correspondence address*** --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-18, 28, and 29* is/are pending in the application.

4a) Of the above, claim(s) *1, 2, 8, 11, 14-18, 28, and 29* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *3-7, 9, 10, 12, and 13* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Interview Summary

Application No.	Applicant(s)	Examiner	Art Unit
09/915,694	Bandman et al.	Christian L. Fronda	1652

All participants (applicant, applicant's representative, PTO personnel):

(1) *Christian L. Fronda* [signature] (3) ____

(2) *Debbie Ellis* (4) ____

Date of Interview *Jul 2, 2002*

Type: a) ☒ Telephonic b) ☐ Video Conference
c) ☐ Personal [copy is given to 1) ☐ applicant 2) ☐ applicant's representative]

Exhibit shown or demonstration conducted: d) ☐ Yes e) ☒ No. If yes, brief description:

Claim(s) discussed: *None*

Identification of prior art discussed:
None

Agreement with respect to the claims f) ☐ was reached. g) ☒ was not reached. h) ☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments:

The requirements stated in the office communication Notice to Comply with Requirements dated 06/03/2002 (Paper No.7) have been withdrawn.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

i) ☒ It is not necessary for applicant to provide a separate record of the substance of the interview (if box is checked).

Unless the paragraph above has been checked, THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached

[signature]

PONNATHAPURA ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

Examiner's signature, if required

DETAILED ACTION

Election/Restriction

1. Applicants' election with traverse of Group II (claims 3-7, 9, 10, 12, and 13) in Paper No. 6 is acknowledged. The traversal is on the grounds that the claims of Group II drawn to a polynucleotide and the claims of Groups III-VIII could be examined at the same time because the searches for each invention would overlap and would pose no undue burden to search; the claims of Groups V-VIII are method claims which depend from the polynucleotide of Group II and should be rejoined upon allowance of the polynucleotide of Group II; a search for the polynucleotide of Group II would overlap with a search for the transgenic organism of Group III; and a search for the polynucleotide of Group II would overlap with a search for the antibody of Group IV.

Applicants' argument that a search of all the claims of Groups I-VIII would pose no undue burden is not found persuasive because the polypeptide of Group I, the polynucleotide of Group II, the transgenic organism of Group III, and the antibody of Group IV are each independent chemical entities and require different literature searches as shown by their different classification stated in the Office Action dated 02/07/2002 (Paper No. 5), and a search of the products of Groups I-IV in the patent literature and the non-patent literature cannot be made without serious burden because the products require separate searches that have different limits, boundaries, scope, and subject matter. As stated in the Office Action dated 02/07/2002 (Paper No. 5), each of the processes of Groups V-VIII are distinct both physically and functionally, have different purposes, require different process steps, reagents, and parameters, and a search of each of the processes of Groups V-VIII would require searches that have different limits, boundaries, scope, and subject matter.

Applicants' argument that a search for the polynucleotide of Group II would overlap with a search for a transgenic organism of Group III is not found persuasive because the polynucleotide of Group II and the transgenic organism of Group III are each independent chemical entities and require different literature searches as shown by their different classification stated in the Office Action dated 02/07/2002 (Paper No. 5), and a search of the polynucleotide of Group II and the transgenic organism of Group III in the patent literature and the non-patent literature cannot be made without serious burden because the products require separate searches that have different limits, boundaries, scope, and subject matter.

Applicants' argument that a search for the polynucleotide of Group II would overlap with a search for the antibody of Group IV is not found persuasive because the polynucleotide of Group II and the antibody of Group IV are each independent chemical entities and require are each independent chemical entities and require different literature searches as shown by their different classification stated in the Office Action dated 02/07/2002 (Paper No. 5), and a search

of the polynucleotide of Group I and the antibody of Group IV in the patent literature and the non-patent literature cannot be made without serious burden because the products require separate searches that have different limits, boundaries, scope, and subject matter.

The requirement is still deemed proper for the reasons stated above and of record, and is therefore made FINAL.

2. Claims 3-7, 9, 10, 12, and 13 are under consideration in this Office Action.

Nucleotide Sequence and/or Amino Acid Disclosures

3. The requirements stated in the communication "Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures" dated 06/03/2002 (Paper No. 7) have been withdrawn.

Claim Objections

4. Claims 3-7, 9, and 10 are objected to because of the following informalities: the claims are objected to because they depend from non-elected claims 1 or 2. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. For examination purposes, it is assumed that claims 3-7, 9, and 10 recite all the limitations of claims 1 or 2.

Claim Rejections - 35 U.S.C. § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 3-7, 9, 10, 12, and 13 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Applicant discloses the nucleotide sequences of SEQ ID NO: 2 and the deduced amino acid sequence of SEQ ID NO: 1. Applicants state that the protein consisting of SEQ ID NO: 1 is a malate dehydrogenase which is a generic asserted utility. The specification does not specifically disclose the function/activity of the protein consisting of SEQ ID NO: 1. The specification does not show any enzyme assays that demonstrate that the protein consisting of SEQ ID NO: 1 has malate dehydrogenase activity. There is no disclosed or "real world" utility associated with the nucleic acid of SEQ ID NO: 2 or the protein of SEQ ID NO: 1. It appears that the main utility of the nucleic acid and protein is to carry out further research to identify the biological function associated with the nucleic acid and protein. Substantial utility defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utility. Thus, the claimed invention has no specific and substantial asserted utility or a well established utility.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 3-7, 9, 10, 12, and 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention encompass any polynucleotide encoding any naturally occurring polypeptide comprising an amino acid sequence at least 90% identical to SEQ ID NO: 1 or SEQ ID NO: 2, any polynucleotide encoding any polypeptide comprising SEQ ID NO: 1 or SEQ ID NO: 2, any polynucleotide encoding any biologically active fragment of a polypeptide having an amino acid sequence of SEQ ID NO: 1, any polynucleotide encoding any immunogenic fragment of a polypeptide having an amino acid sequence of SEQ ID NO: 1, any polynucleotide comprising at least 60 contiguous nucleotides of SEQ ID NO: 2 or a polynucleotide that is 90% identical to SEQ ID NO: 2. The specification, however, only provides the following representative species encompassed by the invention: an isolated polynucleotide consisting of SEQ ID NO: 2. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative

species of these polynucleotides by any identifying structural characteristics or properties for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

9. Claims 3-7, 9, 10, 12, and 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 3-7, 9, 10, 12, and 13 are rejected under 35 U.S.C. 112, first paragraph, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, the claims encompass any polynucleotide encoding any naturally occurring polypeptide comprising an amino acid sequence at least 90% identical to SEQ ID NO: 1 or SEQ ID NO: 2, any polynucleotide encoding any polypeptide comprising SEQ ID NO: 1 or SEQ ID NO: 2, any polynucleotide encoding any biologically active fragment of a polypeptide having an amino acid sequence of SEQ ID NO: 1, any polynucleotide encoding any immunogenic fragment of a polypeptide having an amino acid sequence of SEQ ID NO: 1, any polynucleotide comprising at least 60 contiguous nucleotides of SEQ ID NO: 2 or a polynucleotide that is 90% identical to SEQ ID NO: 2.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The specification provides guidance and examples for making an isolated polynucleotide consisting of SEQ ID NO: 2. However, the specification does not teach the specific structural/catalytic amino acids and the structural motifs essential for protein activity/function which cannot be altered. The state of the art as exemplified by Attwood et al. (Comput. Chem. 2001, Vol. 25(4), pp. 329-39) is such that "...we do not fully understand the rules of protein folding, so we cannot predict protein structure; and we cannot invariably diagnose protein function, given knowledge only of its sequence or structure in isolation" (see Abstract and entire publication). Furthermore, Ponting (Brief. Bioinform. March 2001, Vol. 2(1), pp. 19-29) states that "...predicting function by homology is a qualitative, rather than quantitative, process and requires particular care to be taken...due attention should be paid to all available clues to

function, including orthologue identification, conservation of particular residue types, and the co-occurrence of domains in proteins" (See Abstract and entire publication).

The standard for meeting the enablement requirement is whether one of skill in the art can make the invention without undue experimentation. The amount of experimentation to make the claimed polynucleotide is enormous and entails selecting specific nucleotides to change (deletion, insertion, substitution, or combinations thereof) in a polynucleotide to make a polynucleotide encoding any naturally occurring polypeptide comprising an amino acid sequence at least 90% identical to SEQ ID NO: 1 or SEQ ID NO: 2, a polynucleotide encoding any polypeptide comprising SEQ ID NO: 1 or SEQ ID NO: 2, a polynucleotide encoding any biologically active fragment of a polypeptide having an amino acid sequence of SEQ ID NO: 1, a polynucleotide encoding any immunogenic fragment of a polypeptide having an amino acid sequence of SEQ ID NO: 1, any polynucleotide comprising at least 60 contiguous nucleotides of SEQ ID NO: 2 or a polynucleotide that is 90% identical to SEQ ID NO: 2 and determining by assays whether the encoded polypeptide has malate dehydrogenase activity.

The specification does not provide guidance with respect to the specific structural/catalytic amino acids and the structural motifs essential for enzyme structure and activity/function which must be preserved. Thus, searching for the specific nucleotides to change (deletion, insertion, substitution, or combinations thereof) in a polynucleotide to make the claimed polynucleotide is well outside the realm of routine experimentation and predictability in the art of success in determining whether the resulting polypeptide has activity is extremely low since no information is provided by the specification regarding the specific catalytic amino acids and the structural motifs essential for enzyme structure and activity/function which must be preserved.

The Examiner finds that one skilled in the art would require additional guidance, such as information regarding the specific catalytic amino acids and the structural motifs essential for activity/function which must be preserved. Without such a guidance, the experimentation left to those skilled in the art is undue.

Claim Rejections - 35 U.S.C. § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claim 3 is rejected under 35 U.S.C. 102(b) as being anticipated by Joh et al. (Accession M16229).

Joh et al. (Accession M16229) teach a polynucleotide that encodes a malate dehydrogenase comprising an amino acid sequence that is 94.675% identical to SEQ ID NO: 1 (see attached alignment). Thus, the reference teachings anticipate the of claimed invention.

12. Claim 13 is rejected under 35 U.S.C. 102(b) as being anticipated by Hudson ~~et al~~: (Accession G26455).

Hudson ~~et al.~~ (Accession G26455) teach a polynucleotide that contains at least 100 contiguous nucleotides of SEQ ID NO: 2 (see attached alignment). Thus, the reference teachings anticipate the of claimed invention.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L. Fronda whose telephone number is (703)305-1252. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703)308-3804. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703)308-0196.

CLF

PONNATHAPURA ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600